1: Semin Interv Cardiol 2000 Sep;5(3):109-115 Related Articles

Pathophysiology of coronary thrombosis.

Kristensen SD, Lassen JF, Ravn HB.

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Detailed knowledge of the pathophysiology as well as the dynamic nature of c thrombus formation provides a valuable tool for correct management and pro adjunctive therapy in patients with acute coronary syndromes. Coronary thror in the majority of cases caused by disruption or fissuring of an atherosclerotic At the lesion thrombogenic material will be exposed to the flowing blood lead activation of platelets and the formation of a platelet clot. Simultaneously, the coagulation system is activated resulting in increased thrombin formation. Thr is a key mediator in arterial thrombosis, due to its effect on both platelets and generation. Thrombin contributes to the stabilization of an initially loose plate by generating cross-bound fibrin within the thrombus. During the course of ar coronary syndrome, the patient presents changing chest pain and dynamic isch ECG findings. This is likely to be related to the dynamic nature of the pathophysiology. The presence of a non-occlusive coronary thrombus may de the myocardium its normal blood flow and oxygen supply, leading to ischaem During lysis or embolization, blood supply may be restored, but the presence thrombus fragments in the microcirculation holds the potential to sustained interference with myocardial metabolism. The emboli contain activated platele which release vasoconstrictors that may compromise the microcirculation. Rec thrombus formation at the lesion site may result in occlusion of the artery add the dynamic nature of the clinical presentation. In conclusion, platelets, the coagulation system, and the endothelium cause a dynamic process of intermitt occlusion, vasospasm and embolization of thrombus material.

Publication Types:
- Review
- Review, tutorial

PMID: 11054908 [PubMed - indexed for MEDLINE]

1: Ann Med 2000 Nov;32(8):561-571 Related Articles

Antiplatelet medications and their indications in preventing an treating coronary thrombosis.

Van De Graaff E, Steinhubl SR.

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Platelets play a pivotal role in the pathophysiology of unstable angina, acute myocardial infarction, and complications following percutaneous coronary intervention. Three classes of platelet-inhibiting drugs, aspirin, thienopyridines platelet glycoprotein IIb/ IIIa inhibitors, are now commonly used for the preve and treatment of disorders of coronary artery thrombosis. For the last several aspirin has been the sole option for antiplatelet therapy in the treatment and prevention of the manifestations of cardiovascular disease. However, a wider selection of antiplatelet agents, including the thienopyridines (ticlopidine and clopidogrel) and the platelet glycoprotein (GP)IIb/IIIa receptor antagonists, a available and provide clinicians with the opportunity to potentially improve up previous gold standard of aspirin. This review summarizes these drugs and the scientific data that have led to their use in primary and secondary prevention, angina, myocardial infarction, and percutaneous coronary intervention.

Publication Types:
- Review
- Review, tutorial

PMID: 11127934 [PubMed - indexed for MEDLINE]

1: Hosp Med 2000 Sep;61(9):628-636 Related Articles, Books,

Management of venous and cardiovascular thrombosis: enoxap

Harvey DM, Offord RH.

Department of Haematology, Northwick Park Hospital NHS Trust, Harrow, Middlesex.

Enoxaparin has strong clinical evidence that supports its license in a broad spe of therapeutic indications, including thromboprophylaxis in surgical patients, i patients bedridden because of acute illness, the once-daily treatment of venou thromboembolism and the treatment of unstable angina and non-Q wave myoc infarction.

Publication Types:
- Review
- Review, tutorial

PMID: 11048604 [PubMed - indexed for MEDLINE]

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1: Trans Am Clin Climatol Assoc 2000;111:158-163 Related Articles

Nitric oxide insufficiency and arterial thrombosis.

Loscalzo J, Freedman J, Inbal A, Keaney JF Jr, Michelson AD, Vita JA.

Evans Department of Medicine, Boston University School of Medicine, Massachusetts 02118-2394, USA.

Publication Types:
- Review
- Review, tutorial

PMID: 10881340 [PubMed - indexed for MEDLINE]

Direct thrombin inhibitors for treatment of arterial thrombosis potential differences between bivalirudin and hirudin.

Bates SM, Weitz JI.

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Given the central role of thrombin in arterial thrombogenesis, most treatment strategies for acute coronary syndromes are aimed at inhibiting its generation blocking its activity. Although heparin has been widely used, it has limitations setting of arterial thrombosis. These limitations reflect the inability of heparin inactivate thrombin bound to fibrin, a major stimulus for thrombus growth. In addition, the anticoagulant response to heparin varies from patient to patient, heparin is neutralized by platelet Factor IV, large quantities of which are relea from platelets activated at sites of plaque rupture. Consequently, heparin requ careful laboratory monitoring to ensure an adequate anticoagulant effect. Dire thrombin inhibitors, such as hirudin and bivalirudin, overcome the limitations heparin. These agents inhibit fibrin-bound thrombin, as well as fluid-phase thr and produce a predictable anticoagulant response. Bivalirudin has both safety potential efficacy advantages over hirudin. Bivalirudin appears to have a wider therapeutic window than hirudin, possibly because bivalirudin only transiently the active site of thrombin. The better safety profile of bivalirudin permits administration of higher doses, which may give it an efficacy advantage. Hiruc prevents thrombin from activating protein C, thereby suppressing this natural anticoagulant pathway. In contrast, bivalirudin may promote protein C activat transiently inhibiting thrombin until it can be bound by thrombomodulin. Diffe between bivalirudin and hirudin, as well as other direct thrombin inhibitors, hi the pitfalls of considering all direct thrombin inhibitors to have equivalent risk profiles

Publication Types:
- Review
- Review, tutorial

PMID: 9809887 [PubMed - indexed for MEDLINE]

1: Nephron 1993;63(3):273-278 Related Articles

Plasma parameters of the prothrombotic state in chronic urem

Sagripanti A, Cupisti A, Baicchi U, Ferdeghini M, Morelli E, Barsotti G

Istituto Clinica Medica I, Universita di Pisa, Italy.

We measured plasma parameters of the prothrombotic state, namely thrombin-antithrombin III complex (TAT), fibrinopeptide A (FPA). D-dimer (von Willebrand factor (vWF), tissue-type plasminogen activator (tPA), beta-thromboglobulin (beta TG), platelet factor 4 (PF4) and serotonin (5HT) series of 51 adult patients with chronic uremia: 22 were on maintenance hemc (MHD) and 29 on conservative dietary treatment. Serum tumor necrosis factc (TNF) was determined as well. Uremics presented significantly higher levels c FPA, DD, vWF, TNF, beta TG and 5HT than normal controls. Patients on conservative treatment showed lower levels of TAT, DD, TNF and beta TG th patients on MHD. Our results provide evidence that a prothrombotic state exi chronic uremia and that MHD patients have a higher degree of hypercoagulat Both hemodialysis procedure and uremia-related factors are likely to contribu hemostatic derangement.

PMID: 8446263 [PubMed - indexed for MEDLINE]

1: Kidney Int 1992 Nov;42(5):1124-1129 Related Articles

Procoagulant effect of the OKT3 monoclonal antibody: involve of tumor necrosis factor.

Pradier O, Marchant A, Abramowicz D, De Pauw L, Vereerstraeten P, Kinnaert P, Vanherweghem JL, Capel P, Goldman M.

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We recently observed that the prophylactic administration of high doses of OI monoclonal antibody (MoAb) in cadaveric renal transplantation favors the development of thromboses of the grafts' main vessels and of thrombotic microangiopathies. These clinical observations led us to perform sequential determinations of plasma levels of prothrombin fragment 1 and 2 (F 1 + 2) an degradation products (FDP) after the first injection of 5 or 10 mg OKT3 give prophylaxis in kidney transplant recipients. The values observed have been co with those of kidney transplant recipients not treated with OKT3. F 1 + 2 leve peaked four hours after the first injection of 5 mg OKT3 (mean +/- SEM: 4.8 0.73 vs. 1.75 +/- 0.37 nmol/liter in controls, $P < 0.01$), indicating activation o common pathway of the coagulation cascade. FDP levels were already above values at four hours and continued to increase until 24 hours (mean +/- SEM a 4729 +/- 879 vs. 1038 +/- 320 ng/ml in controls, $P < 0.05$), indicating a fibrin process. The magnitude and the time course of the changes in F 1 + 2 and FD plasma levels were similar whether the patients received 5 or 10 mg dose of C The levels of von Willebrand factor (VWF) antigen, a molecule released by ac or damaged endothelial cells, were also significantly increased after injection ((mean +/- SEM at 24 hr, 3.67 +/- 0.18 vs. 2.17 +/- 0.11 U/ml in controls, P < The procoagulant effects of OKT3 were further investigated in vitro on huma umbilical vein endothelial cells (HUVEC).(ABSTRACT TRUNCATED AT 2 WORDS)

Publication Types:
- Clinical trial
- Controlled clinical trial

PMID: 1453598 [PubMed - indexed for MEDLINE]

1: Arteriosclerosis 1990 Jan;10(1):49-61 Related Articles

Activation of endothelial cells induces platelet thrombus forma on their matrix. Studies of new in vitro thrombosis model with molecular weight heparin as anticoagulant.

Zwaginga JJ, Sixma JJ, de Groot PG.

Department of Hematology, University Hospital, Utrecht, The Netherlands.

Previous studies have indicated that activation of endothelial cells may lead to production of tissue factor. We have studied the effect of endothelial cell activ and subsequent tissue factor synthesis on thrombus formation on the extracell matrix in flowing blood. Endothelial cells were stimulated with tumor necrosi endotoxin, or phorbol ester. Coverslips with activated cells or their extracellu matrix were introduced into a perfusion system and exposed to blood anticoa with 20 U/ml low molecular weight heparin. This concentration allowed mani of blood without activation of the coagulation cascade. Platelet deposition an formation were evaluated by morphometry, and fibrinopeptide A formation w assayed as a measure of thrombin generation. Activation of endothelial cells ca fibrinopeptide A generation in the perfusate and some deposition of fibrin on endothelial cells; however, platelets were not deposited. The matrix of the stir endothelium also caused enhanced fibrinopeptide A generation, and platelet aggregates and fibrin were deposited on the matrix. Maximal effects were obs with stimulation periods between 4 and 10 hours and were still clearly present 18 hours. Increase in shear rate, perfusion time, and platelet number resulted i increase in platelet adhesion, but platelet aggregate formation as a percentage adhesion remained constant. Platelet aggregate formation and fibrinopeptide A generation were inhibited with antibodies against tissue factor or factor VIIa. aggregate formation alone was inhibited by antibodies against glycoprotein III Polymerization of fibrin on the matrix was best supported in perfusions at a lo rate. The new in vitro thrombosis model presented here provides a powerful t study of the regulation of thrombogeneity by the vessel wall in response to var stimuli.

PMID: 2297347 [PubMed - indexed for MEDLINE]

1: Am J Obstet Gynecol 1995 Dec;173(6):1816-1820 Related Articles, Books,

Am J Obstet Gynecol

Hormone replacement therapy reduces the reactivity of monoc and platelets in whole blood--a beneficial effect on atherogenes thrombus formation?

Aune B, Oian P, Omsjo I, Osterud B.

Department of Obstetrics and Gynecology, University of Tromso, Norway.

OBJECTIVE: Our purpose was to investigate the effects of hormone replacer therapy on the reactivity of monocytes and platelets in whole blood, measurec tissue factor activity, tumor necrosis factor-alpha, and thromboxane B2. STU DESIGN: Thirty-two women were randomized into either transdermal or ora combined hormone replacement therapy and underwent blood sampling before after 3 and 12 months of treatment. The tissue factor activity in monocytes wa measured both in unstimulated whole blood and after a weak lipopolysacchari stimulation. Tumor necrosis factor-alpha and thromboxane B2 formation in pl were measured after a weak lipopolysaccharide stimulation of whole blood. RESULTS: After 12 months of hormone replacement therapy there were sign reductions of tissue factor activity in both unstimulated and lipopolysaccharide-stimulated monocytes ($p < 0.001$) and significant reductio formation of tumor necrosis factor-alpha ($p < 0.03$) and thromboxane B2 ($p <$ There were no differences in these parameters between the transdermal and th groups. No changes were observed after 3 months of therapy. CONCLUSIO Twelve months of hormone replacement therapy reduces cellular activation o monocytes and platelets; these changes may account for some of the beneficia in reducing the risk of cardiovascular disease.

Publication Types:

- Clinical trial
- Randomized controlled trial

PMID: 8610768 [PubMed - indexed for MEDLINE]

1: Am J Cardiol 1991 Sep 3;68(7):36B-50B Related Articles, Books,

Coronary atherosclerotic plaques with and without thrombus in ischemic heart syndromes: a morphologic, immunohistochemic and biochemical study.

Arbustini E, Grasso M, Diegoli M, Pucci A, Bramerio M, Ardissino D, A L, de Servi S, Bramucci E, Mussini A, et al.

Department of Pathology, Universita di Pavia, Italy.

We investigated incidence, severity, and distribution of coronary atherosclero: acute thrombosis, and plaque fissuring in ischemic heart disease (both unstable syndromes and chronic ischemia) and in nonischemic controls. We also studie structural, immunohistochemical, and biochemical profile of plaques, with anc without thrombus, including morphometry, immunophenotyping of inflammat infiltrates, cytokine presence, and ultrastructural features. Critical coronary ste was almost the rule in both acute and chronic ischemic series (greater than 90 whereas it reached 50% in control subjects. Thrombosis was principally chara of unstable-acute ischemic syndromes (unstable angina, 32%; acute myocardia infarction, 52%; cardiac sudden death, 26%) but was also found in chronic isc (stable angina, 12%; ischemic cardiomyopathy, 14%) and in control subjects (Plaque fissuring without thrombus occurred in low percentages in lipid-rich, s eccentric plaques in most series. Major differences were found between pultaceous-rich versus fibrous plaques rather than between plaques with or wi thrombus. Pultaceous-rich plaques were frequent in sites of critical stenosis, thrombosis, and ulceration. Inflammatory infiltrates, i.e., T cells, macrophage: few beta cells, mostly occurred in lipid-rich, plaques unrelated to thrombus. Ir adventitia, infiltrates were a common finding unrelated to any syndrome. Necr cytokines such as alpha-TNF were immunohistochemically detected in macro] smooth muscle, and intimal cells and detected by immunoblotting in 67% of pultaceous-rich plaques, either with or without thrombus. Immune response mediators such as IL-2 were also expressed in analogous plaques but in a min percentage (50%-40%). Media were extensively damaged in severely diseasec with and without thrombus. Ultrastructural study showed that the fibrous cap either highly cellular or densely fibrillar. Intimal injury with collagen exposure often associated with platelet adhesion, whereas foamy cell exposure was not. conclusion, investigated parameters were essentially similar in plaques, both v

without thrombus, whereas major differences were found between pultaceous and fibrous plaques. Since platelets adhere to exposed collagen and not to foa the type of exposed substrates could play a major role in thrombosis.

PMID: 1892066 [PubMed - indexed for MEDLINE]
